## REMARKS

Claims 1 - 15 were presented for examination in this application. The above amendments are provided to more specifically state the Applicants' invention, and to clarify certain steps therein. No new matter has been introduced. Claims 1 - 15 and new claims 16 and 17 remain for examination. In view of the amendments and arguments presented, it is believed that these claims are patentably distinguishable and nonobvious over the cited art and are now in condition for allowance.

Substitute pages 17 to 20, including the claims as amended, are submitted herewith.

LACK OF NOVELTY UNDER PCT ARTICLE 33(2). The Written Opinion states claims 2, 6 and 8 lack novelty under PCT Article 33(2) as being anticipated by El-Ghorr et al. For the following reasons, Applicants respectfully traverse this rejection.

As to claims 6 and 8, Applicants understand the rejection as being based on the dependency from claim 2. That is, claims 6 and 8 would be allowable over this rejection but for the dependency. In order to expedite review and clarify the record, claims 6 and 8 are amended to delete dependency from claim 2, and claims 16 and 17 are added, which are identical to claims 6 and 8 except that they depend solely from claim 2. It is submitted that claims 6 and 8 are accordingly allowable over this rejection, and that new claims 16 and 17 rise or fall with claim 2.

As to claim 2, this claim has been amended to provide that the "composition to be tested" is a "composition to be tested other than inactivated herpes simplex virus". The use of inactivated virus in El-Ghorr et al. was not to test the effectiveness of the composition to inhibit HSV infection, but was rather to mimic some aspects of the natural infection in human subjects by inducing an immune response. See page 489, second column, first paragraph under "Discussion". However, to the extent that such protocol reads on the claim as drafted, the claim has been amended to specifically exclude "inactivated herpes simplex virus" from the compositions to be tested for inhibition. Given that El-Ghorr et al. were using inactivated virus for an entirely different purpose, it is submitted that the amendment overcomes this ground of rejection.

LACK OF INVENTIVE STEP UNDER PCT ARTICLE 33.3. The Written Opinion states claims 1-15 lack an inventive step under PCT Article 33(c) as being obvious over Norval et al. in view of Rooney et al., or Brandt et al., or El-Ghorr et al. For the following reasons, Applicants respectfully traverse this rejection.

As the Written Opinion provides, Norval et al. is solely concerned with developing a model of herpes simplex virus recrudescence, and does not teach testing compounds for their anti-viral efficacy. Thus it is not directly applicable or related to either of Brandt et al. or Rooney et al., which do teaching testing of compounds. Because the art area, and the purpose of the experimentation undertaken, is distinctly different, Applicants traverse the determination that such combination would be "obvious to a person skilled in the art" as required under PCT Article 33(3).

Even if Norval et al. could properly be combined with the other cited art, Norval et al. does not teach elements related to Applicants' invention. Norval et al. specifically requires "u.v.-irradiation before the primary HSV infection..." in order to induce recrudescence in a "proportion of mice." Norval et al., page 2694, second full paragraph. As Norval et al. concludes, that reference "describes a reproducible murine model of recrudescence which involves pre-exposure of animals to an external immunosuppressive signal [u.v.-irradiation] before infection with HSV." Page 2697, first full paragraph. Applicants have amended claims 1, 4 and 5 to specify that the animals are infected with herpes simplex virus "without having prior thereto exposed the animal to localized radiation." Thus Norval et al., by requiring exposure to radiation prior to herpes simplex virus, actually teaches away from Applicants' invention.

With respect to claim 3, Applicants note that this claim involves the step of "determining whether central nervous system damages resulted." It is submitted that no one of the cited references teach or make obvious this step, which evaluates a parameter not described in any of the prior art. This determination involves, as described in Example 26, for example determining inhibition of spinal cord myelitis.

With respect to the El-Ghorr et al. reference, as discussed above the El-Ghorr et al. reference does not teach a "test compound" per se, but merely teaches use of inactivated

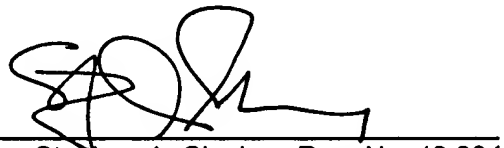
virus for a diff r nt purpose, to induce an immune response. Howev r, claim 2 has been amended to overcome this specific ground of rejection.

With respect to the Brandt et al. and Rooney et al. references, it is submitted that the claims, as amended, overcome any obviousness rejection based upon Norval et al. Norval et al. specifically teaches and requires radiation exposure (an "external immunosuppressive signal") prior to infection, while Applicants teach infection at an abrasion, allowing the abrasion to heal and primary infection to resolve, and thereafter exposing "the area of abrasion to radiation". It should further be noted that Norval et al. appears to teach whole-body irradiation, while Applicants' invention is directed, in claims 1, 4 and 5, to exposure of the area of abrasion to radiation.

CONCLUSION. Withdrawal of the Examiner's rejections of claims 1-15 is respectfully requested, and reconsideration and allowance of claims 1-17 is solicited.

Substitute pages for claims are attached.

Respectfully submitted,



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Date: March 16, 2001

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CLAIMS

What is claimed is:

1. (First Amended) A method of determining the effectiveness of a composition to inhibit herpes simplex virus infection reactivation, comprising the steps of:

a) obtaining one or more animals;

b) creating an abrasion on the animal;

c) inoculating the animal with herpes simplex virus, without having prior thereto exposed the animal to localized radiation, by application of a composition comprising herpes simplex virus to the abrasion, thereby resulting in a primary herpes simplex virus infection in the animal;

d) allowing the abrasion to heal and the primary herpes simplex virus infection to resolve;

e) administering a composition to be tested for inhibition of herpes simplex virus infection reactivation to the animal;

f) exposing the area of abrasion to radiation; and

g) determining whether the herpes simplex virus infection is reactivated.

2. (First Amended) A method of determining the effectiveness of a composition to inhibit herpes simplex virus infection, comprising the steps of:

a) obtaining one or more animals;

b) administering a composition to be tested other than inactivated herpes simplex virus for inhibition of herpes simplex virus infection to the animal;

c) creating an abrasion on the animal;

d) inoculating the animal with herpes simplex virus by application of a composition comprising herpes simplex virus to the abrasion; and

e) determining whether a herpes simplex virus infection resulted.

3. A method of determining the effectiveness of a composition to provide central nervous system protection, comprising the steps of:

a) obtaining one or more animals;

b) administering a composition to be tested to the animal;

c) creating an abrasion on the animal;

d) inoculating the animal with sufficient herpes simplex virus to induce central nervous system damage by application of a composition comprising herpes simplex virus to the abrasion; and

e) determining whether central nervous system damage resulted.

4. (First Amended) A method of determining an effective dose of a composition to inhibit herpes simplex virus reactivation, comprising the steps of:

a) obtaining two or more animals;

b) creating an abrasion on each animal;

c) inoculating each animal with herpes simplex virus, without having prior thereto exposed the animal to localized radiation, by application of a composition comprising herpes simplex virus to the abrasion, thereby resulting in a primary herpes simplex virus infection in each animal;

d) allowing the abrasion of each animal to heal and the primary herpes simplex virus infection to resolve;

e) administering to each animal a selected dose of a composition to inhibit herpes simplex virus infection reactivation;

f) exposing the area of abrasion of each animal to radiation; and

g) determining the rate of reactiviation of the herpes simplex virus infection for each selected dose.

5. (First Amended) A method of determining the effectiveness of an ultraviolet protectant, comprising the steps of:

a) obtaining one or more animals;

b) creating one or more abrasions on the animal;

c) inoculating the animal with herpes simplex virus, without having prior thereto exposed the animal to localized radiation, by application of a composition comprising herpes simplex virus to the abrasion, thereby resulting in a primary herpes simplex virus infection in the animal;

d) allowing the abrasion to heal and the primary herpes simplex virus infection to resolve;

e) administering an ultraviolet protectant to the animal;

f) exposing the area of abrasion to ultraviolet radiation; and

g) determining whether the herpes simplex virus infection is reactivated.

6. (First Amended) The methods of any of claims 1, 3, 4 or 5 wherein the abrasion is a superficial dermabrasion.

7. The methods of any of claims 1 or 4 wherein the radiation is ultraviolet radiation, and is preferably a dose of two MED of ultraviolet-B radiation or solar spectrum ultraviolet radiation.

8. (First Amended) The method of any of claims 1, 3, 4 or 5 wherein the herpes simplex virus is herpes simples virus-1 (HSV-1) or herpes simples virus-2 (HSV-2).

9. The method of any of claims 1, 2 or 4 wherein the herpes simplex virus is a strain isolated from a patient to be treated with a composition to inhibit herpes simplex virus infection reactivation.

10. The method of any of claims 1, 2, 4 or 5 wherein the quantity of HSV applied to the abrasion results in death of approximately 50% of animals administered said quantity of HSV, and is preferably at least one-half log less than the quantity of HSV which results in death of 50% of the animals.

11. The method of any of claims 1, 4 or 5, further comprising the step of determining the severity and duration of herpes simplex virus reactivation infection.

12. The method of claim 4, wherein at least two different selected doses are employed, with each animal administered one selected dose.

13. The method of claim 4, wherein the composition to inhibit herpes simplex virus infection reactivation comprises one or more active ingredients, and the quantity of active ingredient for each selected dose is varied.

14. The method of claim 2, further comprising the steps of:

f) allowing the abrasion to heal;

g) exposing the area of abrasion to ultraviolet radiation; and

h) determining whether a herpes simplex virus infection is reactivated.

15. The method of claim 5, wherein the ultraviolet protectant is a topical composition administered to at least one area of abrasion of the animal.

16. The method of claim 2 wherein the abrasion is a superficial dermabrasion.

17. The method of claim 2 wherein the herpes simplex virus is herpes simples virus-1 (HSV-1) or herpes simples virus-2 (HSV-2)